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Award Number: DAMD17-03-1-0138

TITLE: Cognitive Performance, Quality of Life, and Psychosocial
Adjustment Among Men Receiving Androgen Deprivation
Therapy for Treatment of Prostate Cancer

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REPORT DATE: April 2004

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE			Form Approved OMB No. 074-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE April 2004	3. REPORT TYPE AND DATES COVERED Annual (1 Apr 2003 - 31 Mar 2004)		
4. TITLE AND SUBTITLE Cognitive Performance, Quality of Life, and Psychosocial Adjustment Among Men Receiving Androgen Deprivation Therapy for Treatment of Prostate Cancer		5. FUNDING NUMBERS DAMD17-03-1-0138		
6. AUTHOR(S) Pamela J. Shapiro, Ph.D.				
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9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSORING / MONITORING AGENCY REPORT NUMBER		
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 Words) Animal models and naturalistic studies of androgen decline in aging men suggest that low testosterone levels contribute to cognitive difficulties. Suppression of testosterone by androgen deprivation therapy (ADT) is the preferred treatment for advanced prostate cancer (PC) and in recent years has been increasingly prescribed for treatment of early stage PC. Although many of the side effects of ADT are well documented, potential cognitive impairment associated with ADT has been neglected in the literature. Our preexisting data indicate that 35% of men receiving ADT report moderate to severe difficulties with attention, concentration, and memory. In addition to normal age-related declines in cognitive function, men receiving ADT may experience hormone-related cognitive impairments that remain undetected and untreated. This study describes the nature and prevalence of objectively assessed cognitive difficulties in PC patients treated with ADT, examines the relationship between subjective reports of cognitive impairment and objective measurement of cognitive performance, and assesses relationships among fatigue, psychological distress, and cognitive function. Preliminary results show that 58% of the men have cognitive deficits ≥ 1 SD below age- and education-adjusted population norms in one or more cognitive domains, and 92% have at least one area of performance ≥ 1 SD below expected functioning based on estimated premorbid IQ.				
14. SUBJECT TERMS Prostate Cancer, Cognitive Function, Quality of Life, Testosterone			15. NUMBER OF PAGES 7	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

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Introduction

This project is an individual postdoctoral training grant in prostate cancer. The project involves focused mentorship and training in all aspects of prostate cancer, including psychosocial and quality of life issues. The training plan includes opportunities for secondary data analyses as well as an original research project focusing on neurocognitive sequelae of androgen deprivation therapy (ADT). Suppression of testosterone by androgen deprivation therapy is the preferred treatment for advanced prostate cancer (PC) and in recent years has been increasingly prescribed for treatment of early stage PC. Although many of the side effects of ADT have been well-documented, potential cognitive impairment associated with ADT has been neglected in the literature. In our preexisting pilot data, 35% of men receiving ADT reported moderate to severe difficulties with attention, concentration, and memory, suggesting that in addition to normal age-related declines in cognitive function, men receiving ADT may experience hormone-related cognitive impairments that remain undetected and untreated. The present study describes the nature and prevalence of objectively assessed cognitive difficulties in PC patients treated with ADT, examines the relationship between subjective reports of cognitive impairment and objective measurement of cognitive performance, and assesses relationships among fatigue, psychological distress, quality of life (QoL), and cognitive function.

Body

This project is received notice of award on October 31st, 2002 and notification of final approval on March 1st 2003 stating that the grant contract was signed and scheduled to begin on April 1st, 2003. Preparation for training and research began immediately after the final notification. A list of training and research activities in accord with the original proposal and Statement of Work follows.

Research Progress:

- Initiated start-up meeting with mentors during April. Meet regularly with Drs. Vaughn, Plotkin (now Plotkin -Beister), and Coyne to discuss the research project, current literature, and strategies for future work, presentations, and publications.
- Completed training in neuropsychological assessment and scoring for the specific measures used in this project and consult regularly with Dr. Beister on interpretation of test results.
- Hired and trained research assistant and implemented participant tracking and data management procedures.
- The research project proposed as part of my training is underway. To date we have accrued 19 participants, including 16 men receiving ADT and 3 non ADT controls. We are continuing to accrue patients through Dr. Vaughn's practice and, in an effort to include a greater diversity of men with PC, will now extend recruitment into the larger Penn and Philadelphia communities, including the Veterans Affairs Hospital.

Education and Career Development:

- The abstract for this training grant was accepted for presentation at the March 9th, 2003 American Society for Preventative Oncology New Investigators Workshop. I presented the training goals and background, rationale, and research design of this project, as well as plans for a follow-up study to the senior investigator panel of Patricia Ganz, William Redd, and Alfred Nuegot.
- Attended the newly organized Philadelphia Area Prostate Research (PAPR) Collaborative quarterly meetings from March 2003 to present in order to meet and interact with senior investigators involved in prostate cancer research. This group includes representatives from University of Pennsylvania, Fox Chase Cancer Center, Thomas Jefferson University Cancer Center, and the Lankenau Institute for Medical Research.
- Attended University of Pennsylvania's Abramson Cancer Center Prostate Cancer Conference, *Current Aspects in the Diagnosis and Treatment of Prostate Cancer*, March 28 2003.
- Attended March 2003 Society of Behavioral Medicine Post-Meeting Seminar: *Development and Implementation of a Psychosocial Oncology Program*, March 23rd, 2003.
This program focused on: 1) Critical research and applied issues in psycho-oncology, including primary and secondary prevention, genetic screening, adaptation to cancer, cancer-related fatigue, and cancer-related pain. 2) Pragmatic issues in developing a research and assessment unit, including clinical and neuropsychological assessment and mental health screening, medical staff referral, barriers to referral, and intervention strategies. 3) Measurement issues and appropriate instrumentation to reduce patient burden. 4) Professional issues, including educating medical staff about psychosocial and research issues and educating the psycho-oncology team about medical issues.
- Attend monthly Grand Rounds in Psychiatry, Neuropsychiatry, and Oncology, as well as regular meetings of the Behavioral Oncology Group of the Division of Cancer Control and Outcomes.
- Attended University of Pennsylvania's Interdisciplinary Retreat on Neuroprotection and the Mahoney Institute of Neuroscience Symposium on Brain Research: *From Molecules to Mind*. Relevant talks included presentations on neural substrates of memory and of emotions.
- Attended the NCI Behavioral Research Program sponsored conference, *The Science of Real Time Data Capture: Self-Reports in Health Research*, September 5-7th, 2003. This intensive conference included presentations on design issues, methodology, and statistical challenges unique to ecological momentary assessment (EMA) and electronic diary studies, as well as focused workshops on practical issues implementing EMA studies. My ideas for EMA of cognitive failure events, affect, and fatigue were well received in the workshop, and I am currently working on a design to implement this procedure in men with PC. EMA will allow greater understanding of the specific cognitive difficulties men encounter in daily life and the context in which such events occur.

Key Research Accomplishments

- Secondary data analyses of Dr. Coyne's existing PC database resulted in a first authored paper that is now in press in the journal *Psycho-Oncology*. Overall, results suggest that PC patients on ADT prefer individualized informational support, especially information about treatment and treatment related side-effects. Few participants were interested in psychosocial support, but those who did express interest in psychosocial services were younger and had a shorter duration of ADT. There was substantial interest in Oncolink, an internet-based informational resource, suggesting that the Internet may provide an acceptable mode of service delivery. We recommend that health care providers integrate increased informational support into routine care and consider patient preferences in prioritizing and designing support services.
- Preliminary results of the Prostate Cancer Cognitive Performance (PCCP) study described in the training grant have been presented at the Society of Behavioral Medicine 2004 annual meeting as part of a symposium on quality life in prostate cancer and as a poster at the Abramson Cancer Center's Eunice and Irving Leopold Annual Scientific Symposium and Retreat on March 31st 2004. An updated poster with the most recent participants and data analyses will be presented at the July 2004 American Psychological Association annual convention as part of the Division 38 Health Psychology program.

Publications and Presentations:

- Shapiro, P.J., Coyne, J.C., Kruus, L.K., Palmer, S.C., Malkowicz, S.B., Vaughn, D.J. (in press). Interest in services among prostate cancer patients receiving androgen deprivation therapy. *Psycho-Oncology*.
- Coyne, J.C., Palmer, S.C., Shapiro, P. J. (2004). Prescribing antidepressants to advanced cancer patients with mild depressive symptoms is not justified: Response to Fisch et al. [Letter to the editor]. *Journal of Clinical Oncology*, 22, 205-206.
- Shapiro, P. J. (chair), Diefenbach, M. A., Eton, D. T., & Lepore, S. (2004, March) Factors affecting quality of life among prostate cancer patients: Current knowledge and new directions. [Symposium Abstract] *Annals of Behavioral Medicine*, 27, S169.
- Shapiro, P. J., Coyne, J.C., Butterfield, L. C., Plotkin, R. C., Malkowicz, S. B., & Vaughn, D. J. (2004, March). Cognitive performance, psychological distress, and quality of life among men receiving androgen deprivation therapy for treatment of prostate cancer. [Abstract] *Annals of Behavioral Medicine*, 27, S170.
- Butterfield, L.C., & Shapiro, P.J. (2004, February). *Cognitive complaints, cognitive performance, and psychological distress among men with genitourinary cancers*. Poster presented at the annual meeting of the International Neuropsychological Society, Baltimore.
- Shapiro P.J., Butterfield, L.C., Coyne, J.C., Beister, R.C., Matthews, G., & Vaughn, D.J. (March & July, 2004). *Cognitive Function among Men Receiving Androgen Deprivation Therapy*. Poster to be presented at the Annual Convention of the American Psychological Association and presented at the Eunice and Irving Leopold Annual Scientific Symposium and Retreat, Abramson Cancer Center of the University of Pennsylvania.

- Shapiro, P.J. (2003, March) *Cognitive performance, quality of life, and psychosocial adjustment among men receiving androgen deprivation therapy for treatment of prostate cancer: Design and methods*. Paper presented at the New Investigators Workshop of the annual meeting of American Society of Preventive Oncology, Philadelphia.

Invited Talks:

- *Examining Cognitive Performance among Men Receiving ADT for treatment of Prostate Cancer: Why Prostate Cancer? Why Now?* Talk presented at the Psychosocial-Oncology Seminar at the University Of Pennsylvania School Of Nursing. May 15, 2003.
- *Studying Memory, Attention and Reasoning among Men Treated for Prostate Cancer: Subjective Complaints vs. Objective Measurement*. Talk presented at The University of Pennsylvania Prostate Cancer Support Group. June 17, 2003

Reportable Outcomes

- Preliminary results of the ongoing PCCP study show that 58% of the men had cognitive deficits ≥ 1 SD below age- and education-adjusted population norms in one or more cognitive domains and 92% had at least one area of performance ≥ 1 SD below expected functioning based on estimated premorbid IQ. Self-reports of poor cognitive function were related to increased psychological distress and decreased physical and emotional QOL. Although 83% of men reported some cognitive difficulties, cognitive complaints were unrelated to objective cognitive performance. Men who were clinically distressed reported substantially greater subjective cognitive difficulties and decreased overall QoL. Objective measures of fatigue (reaction time and lapses) were associated with poorer cognitive performance.
- The majority of men in this sample experienced mild cognitive deficits across domains and should be reevaluated for further decline in two years. Cognitive remediation should be offered to men with clinically relevant mild cognitive impairment (MCI). Cognitive complaints among PC patients may indicate the presence of psychological distress, and patients reporting cognitive difficulties should be evaluated for psychiatric comorbidity and treated accordingly. Treatment of psychological distress may reduce cognitive symptoms and improve overall QoL.

Conclusions

Progress on the training grant and the associated research project continues. Although, as seen above, we are finding cognitive deficits among men treated with ADT, these results are still preliminary and are primarily descriptive. Until we have a larger sample and adequate numbers of control patients, no inferences about the relationship of ADT to these deficits can be made.

References None

Appendices None